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FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, CANCERLIT, BIOTECHDS' ENTERED AT  
14:53:09 ON 04 JUN 2003

L1 3099 S 100K OR NUCLEOTID? 9###  
L2 109595 S ADENOVIR?  
L3 246 S L2 AND L1  
L4 82 DUP REM L3 (164 DUPLICATES REMOVED)  
L5 2315221 S DELE? OR REMOV?  
L6 632978 S DEFICIENT OR LACKING  
L7 2890079 S L6 OR L5  
L8 16 S L7 AND L4

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| L3 with l2 | 22        |

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L4

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DB=USPT,PGPB,JPAB,EPAB,DWPI; PLUR=YES; OP=ADJ

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|-----------|---|-------|-----------|
| <u>L4</u> | L3 with l2                                  | 22    | <u>L4</u> |
| <u>L3</u> | adenovi\$                                   | 22259 | <u>L3</u> |
| <u>L2</u> | 100K or nucleotide 9??? or nucleotides 9??? | 6045  | <u>L2</u> |
| <u>L1</u> | 100K or nucleotide 9???                     | 6045  | <u>L1</u> |

END OF SEARCH HISTORY

L8 ANSWER 13 OF 16 CAPLUS COPYRIGHT 2003 ACS  
 AN 2000:161478 CAPLUS  
 DN 132:204060  
 TI **Adenoviruses deleted** in the IVa2, 100K  
 and/or preterminal protein sequences  
 IN Amalfitano, Andrea; Chen, Yuan Tsong; Hu, Huimin  
 PA Duke University, USA  
 SO PCT Int. Appl., 156 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 FAN.CNT 1

|      | PATENT NO.      | KIND   | DATE     | APPLICATION NO. | DATE     |
|------|-----------------|--|----------|-----------------|----------|
| PI   | WO 2000012740   | A2   | 20000309 | WO 1999-US19540 | 19990827 |
|      | WO 2000012740   | A3   | 20001123 |                 |          |
|      | W:              | AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM |          |                 |          |
|      | RW:             | GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG   |          |                 |          |
|      | CA 2340276      | AA   | 20000309 | CA 1999-2340276 | 19990827 |
|      | AU 9956942      | A1   | 20000321 | AU 1999-56942   | 19990827 |
|      | EP 1108049      | A2   | 20010620 | EP 1999-943952  | 19990827 |
|      | R:              | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO   |          |                 |          |
|      | US 6328958      | B1   | 20011211 | US 1999-384749  | 19990827 |
|      | JP 2002528056   | T2   | 20020903 | JP 2000-567725  | 19990827 |
| PRAI | US 1998-145742P | P  | 19980828 |                 |          |
|      | WO 1999-US19540 | W  | 19990827 |                 |          |

AB The present invention provides **deleted adenovirus** vectors. The inventive **adenovirus** vectors carry one or more **deletions** in the IVa2, 100K, polymerase and/or preterminal protein sequences of the **adenovirus** genome. In the human **adenovirus** serotype 5 genomes, such **deletions** are at nucleotide positions 4830-5766, 24,990-25,687, and/or 7274-7991. The **adenoviruses** may addnl. contain other **deletions**, mutations or other modifications as well. In particular preferred embodiments, the **adenovirus** genome is multiply **deleted**, i.e., carries 2 or more **deletions** therein. The **deleted adenoviruses** of the invention are "propagation-defective" in that the virus cannot replicate and produce new virions in the absence of complementing function(s). Preferred **adenovirus** vectors of the invention carry a heterologous nucleotide sequence encoding a protein or peptide assocd. with a metabolic disorder, more preferably a protein or peptide assocd. with a lysosomal or glycogen storage disease, most preferably, a lysosomal acid .alpha.-glucosidase. The **deleted adenovirus** vectors advantageously have an increased carrying capacity for heterologous nucleotide sequences, demonstrate lower levels of viral protein expression, induce fewer host immune responses, and/or exhibit increased stability and prolonged transgene expression when introduced into target cells.

L8 ANSWER 11 OF 16 CAPLUS COPYRIGHT 2003 ACS

AN 2002:946147 CAPLUS

DN 138:34131

TI Helper-virus independent replicating **adenovirus** vectors with  
**100K** or Elb gene **deletion** for gene therapy

IN Amalfitano, Andrea; Hodges, Bradley L.

PA Duke University, USA; Koeberl, Dwight D.

SO PCT Int. Appl., 75 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

|      | PATENT NO.   | KIND   | DATE     | APPLICATION NO. | DATE     |
|------|--|--|----------|-----------------|----------|
| PI   | WO 2002098466  | A1   | 20021212 | WO 2002-US17070 | 20020531 |
|      | W:   | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM |          |                 |          |
|      | RW:  | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG   |          |                 |          |
| PRAI | US 2001-295914P  | P  | 20010604 |                 |          |
| AB   | The present invention provides replicating [ <b>100K</b> -]<br><b>adenovirus</b> vectors that have an impairment in <b>100K</b><br>activity. In particular preferred embodiments, the impairment is the<br>result of a <b>deletion</b> in the <b>100K</b> coding region of the<br><b>adenovirus</b> vector genome. It is further preferred that the<br><b>adenovirus</b> produces the El gene products. In an alternate<br>embodiment, the <b>adenovirus</b> produces the Ela gene products, but<br>has an impairment in the Elb coding region, such that replication of the<br>virus is limited to p53- cells. Also described are methods of making and<br>administering the inventive <b>adenovirus</b> vectors to a cell or to a<br>subject. Further provided is use of the inventive [ <b>100K</b> -] Ad<br>vectors as a helper virus for the prodn. of vector stocks of adeno-assocd.<br>virus. |  |          |                 |          |

L8 ANSWER 7 OF 16 MEDLINE  
 AN 83303837 MEDLINE  
 DN 83303837 PubMed ID: 6612996  
 TI Analysis of Ad5 hexon and **100K** ts mutants using  
 conformation-specific monoclonal antibodies.  
 AU Cepko C L; Sharp P A  
 NC NIH-P01-CA14051 (NCI)  
 P01-CA26717 (NCI)  
 SO VIROLOGY, (1983 Aug) 129 (1) 137-54.  
 Journal code: 0110674. ISSN: 0042-6822.  
 CY United States  
 DT Journal; Article; (JOURNAL ARTICLE)  
 LA English  
 FS Priority Journals  
 EM 198310  
 ED Entered STN: 19900319  
 Last Updated on STN: 19970203  
 Entered Medline: 19831008  
 AB **Adenovirus** type 5 ts mutants **deficient** in hexon  
 metabolism were investigated using conformation-specific monoclonal  
 antibodies directed against hexon capsomeres and the viral **100K**  
 protein. The ts mutants map either in the hexon structural gene or in the  
 gene encoding the **100K** protein, a major, late nonstructural  
 protein. All of the mutants examined (ts1, ts2, ts3, ts4, ts17, and ts20  
 of J. F. Williams, M. Gharpure, S. Ustacelebi, and S. McDonald  
 (1971). J. Gen. Virol. 11, 95-101) were unable to produce the  
 capsomeric form of hexon (a trimer of three hexon monomers) at the  
 nonpermissive temperature. However, all of the mutants retained the  
 ability to produce a complex of **100K** and hexon which has been  
 demonstrated to play a major role in the assembly of hexon trimers. The  
 mutants accumulated nontrimerized hexon in this ts complex in the  
 perinuclear region of the cell. Several of the mutants (ts1, ts2, ts3)  
 were found to successfully assemble hexon synthesized at the nonpermissive  
 temperature upon shift down to the permissive temperature, even in the  
 presence of a protein synthesis inhibitor. The mutant, ts2, which maps in  
 the hexon structural gene, was found to be dependent on protein synthesis  
 for transport of hexon trimers into the nucleus during temperature shift  
 down, while the **100K** ts mutants, ts1 and ts3, were independent  
 of protein synthesis for both hexon assembly and transport.

L8 ANSWER 1 OF 16 MEDLINE  
 AN 2001320301 MEDLINE  
 DN 21286721 PubMed ID: 11390592  
 TI **Adenovirus** vectors with the **100K** gene **deleted**  
 and their potential for multiple gene therapy applications.  
 AU Hodges B L; Evans H K; Everett R S; Ding E Y; Serra D; Amalfitano A  
 CS Department of Pediatrics, Division of Medical Genetics, Duke University  
 Medical Center, Durham, NC 27710, USA.  
 NC DK52925 (NIDDK)  
 SO JOURNAL OF VIROLOGY, (2001 Jul) 75 (13) 5913-20.  
 Journal code: 0113724. ISSN: 0022-538X.  
 CY United States  
 DT Journal; Article; (JOURNAL ARTICLE)  
 LA English  
 FS Priority Journals  
 EM 200106  
 ED Entered STN: 20010702  
 Last Updated on STN: 20010702  
 Entered Medline: 20010628  
 AB The **100K** protein has a number of critical roles vital for  
 successful completion of the late phases of the **adenovirus** (Ad)  
 life cycle. We hypothesized that the introduction of **deletions**  
 within the **100K** gene would allow for the production of a series  
 of new classes of Ad vector, including one that is replication competent  
 but blocked in the ability to carry out many late-phase Ad functions.  
 Such a vector would have potential for several gene therapy applications,  
 based upon its ability to increase the copy number of the transgene  
 encoded by the vector (via genome replication) while decreasing the side  
 effects associated with Ad late gene expression. To efficiently produce  
**100K-deleted** Ad ([**100K**-]Ad) vectors, an E1-  
 and **100K**-complementing cell line (K-16) was successfully  
 isolated. Transfection of an [E1-,**100K**-]Ad vector genome into  
 the K-16 cells readily yielded high titers of the vector. After infection  
 of noncomplementing cells, we demonstrated that [**100K**-]Ad  
 vectors have a significantly decreased ability to express several Ad late  
 genes. Additionally, if the E1 gene was present in the infected  
 noncomplementing cells, [**100K**-]Ad vectors were capable of  
 replicating their genomes to high copy number, but were significantly  
 blocked in their ability to efficiently encapsidate the replicated  
 genomes. Injection of an [E1-,**100K**-]Ad vector in vivo also  
 correlated with significantly decreased hepatotoxicity, as well as  
 prolonged vector persistence. In summary, the unique properties of [  
**100K**-]Ad vectors suggest that they may have utility in a variety  
 of gene therapy applications.

**WEST**

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L4: Entry 3 of 22

File: USPT

Dec 10, 2002

DOCUMENT-IDENTIFIER: US 6492343 B1

TITLE: Porcine adenovirus type 3 genome

Other Reference Publication (3):

McCoy et al. Nucleotide and Amino Acid Sequence Analysis of the 100K Protein of a Serotype 3 Porcine Adenovirus. DNA Sequence-The Journal of Sequencing and Mapping, vol. 8, pp. 59-61, 1997.\*